

REMARKS

Rejections under §112, second paragraph

It is believed that the claims as written were clear to the skilled worker; however, to clarify them in view of the §112, second paragraph issues raised in the Office action, the enclosed amendments have been made. These amendments do not change the claim scope, or the scope of the dependent claims which have been thereby added.

Rejection under §§102 and 103 over Han et al. (*J. Bio. Chem.*, 272:28660-65, 1997)

Han et al. do not anticipate or suggest the claimed invention. The general point of this publication was to show that heparin cofactor II ("HCII") inhibits meizothrombin and meizothrombin (desF1) in the presence of dermatan sulfate, to elucidate the kinetics of this process, and to show that the transformation of thrombin to prothrombin was blocked by HCII. There is no disclosure in Han et al. related to the usefulness of the disclosed chemical compounds for measuring unknown inhibitor concentrations, let alone for assembling these compounds into a single test kit package.

Moreover, Han et al. do not disclose a single test kit package comprising a standard curve for determining the amount of a thrombin inhibitor in a sample. See, e.g., Claims 14, 16, and 18. Since the only teaching in the disclosure is of using known amounts of known compounds (see, e.g., Fig. 2 and Table I), there would have been no motivation to have included a standard curve for determining unknown concentrations.

Rejection under §103 over U.S. Pat. No. 5,547,850 in light of U.S. Pat. No. 5,702,912 or Houbouyan et al. (*Blood Coag. Fibrin.* 7:24-30, 1996)

The combination of references cited in the Office action does not render the claimed invention obvious. U.S. Pat. No. 5,547,850 ("the '850 patent") is described in the present specification, e.g., Page 2, beginning on line 23. As indicated therein, the '850 patent does not disclose a chromogenic/fluorogenic substance capable of being dissociated by meizothrombin or

meizothrombin-des fragment 1. The method described in the '850 patent is based on a different principal in which the delay in coagulation is used as a measure of inhibition. See, the '850 patent, e.g., Abstract; Summary of the Invention. U.S Pat. No. 5,702,912 ("the '912 patent") and Houbouyan et al., on the other hand, refer to such a chromogenic/fluorogenic substance, but do not disclose whether meizothrombin or meizothrombin-des fragment 1 would be capable of dissociating it.

Thus, there is no disclosure in the cited publications that would have motivated a skilled worker to have substituted the chromogenic/fluorogenic substances in the clotting method described by the '850 patent. "Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art." M.P.E.P. 2143.01.

Moreover, these cited publications do not provide an expectation of success, e.g., whether the substances described in the '912 patent and/or Houbouyan et al. would have been dissociated by meizothrombin or meizothrombin-des fragment 1. Obviousness also requires a reasonable expectation of success. See, e.g., M.P.E.P. 2143.02.

Accordingly, withdrawal of the rejection is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,


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